

Applicant(s): Huang et al.  
Application No.: 09/910,887

Docket No.: P444 0001  
GSL/TWB/gl

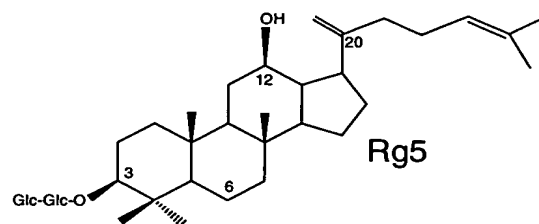
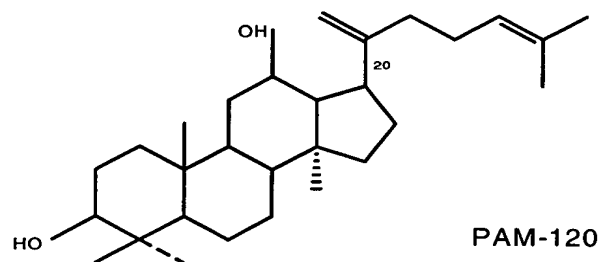
### REMARKS

This amendment is submitted with a Request for Continued Examination and responds to the rejections made by the Examiner in the Final Official Action mailed September 9, 2004. In view of the following remarks and the enclosed inventor Declarations, reconsideration by the Examiner and allowance of the application is respectfully requested.

The Examiner has allowed currently pending claim 10, which is gratefully acknowledged. The Examiner has maintained her rejection of claim 9 under 35 U.S.C. § 103(a) as being unpatentable over Park et al., Yun et al., and Sun Won Kwon et al. On page 3 of the Final Office Action, the Examiner refers to the compounds Rg3, Rh2, and Rg5, which are disclosed in Park et al., Yun et al., and Sun Won Kwon et al. In the Applicant's previous response, the Applicant submitted the affidavit of Dong Huang sworn 10 May 2004 which included evidence of side-by-side experiments conducted to compare the efficacy of PAM-120 with Rg3 and Rh2. A copy of Mr. Huang's affidavit sworn 10 May 2004 is attached hereto as Appendix "B" for the Examiner's reference. The Examiner has found the Applicant's previous arguments persuasive in part.

However, the Examiner has requested that the Applicant conduct side-by-side experiments to compare the activity of Rh5 to PAM-120 (although presumably the Examiner means to request experiments to compare **Rg5** with PAM-120, since Rh5 is not mentioned in the Applicant's previous response as asserted by the Examiner, but rather Rg5 is mentioned in the cited references and in the Examiner's Final Office Action on page 3). The Examiner asserts that the difference between Rh5 (presumably meaning **Rg5**) and PAM-120 is the difference of the moiety at position 3. Applicants respectfully traverse this rejection in view of the enclosed Declaration of Dong Huang sworn 7 March 2005 for the following reasons.

In the prior art compound Rg5, there is an "O-Glc-Glc" moiety at position 3 (see Yun et al. at page S13). In PAM-120, there is a hydroxyl group at position 3. The Applicant has reproduced the compounds below:



Pursuant to 37 CFR 1.132, the Applicant encloses as Appendix "A" the affidavit of Dong Huang, sworn 7 March 2005. In this affidavit, Mr. Huang avers to the results of side-by-side experiments conducted to compare the activity of Rg5 with PAM-120. In paragraph 7, Mr. Huang avers that he conducted an experiment to measure the viability of lung cancer cells in the presence of PAM-120 and Rg5. The results of these experiments are reproduced below in Table 1 for the Examiner's reference.

Table 1: Viability of H460 Lung Cancer Cells in the Presence of 25 uM PAM-120 and Rg5.

Compound (25 uM)	Absorbency of stained cells (M±SD)	Viability (%)
Blank Control	0.352±0.062	100.00
PAM-120	0.218±0.043	61.93
Rg5	0.290±.065	82.38

The lung cancer cells were grown in the presence of PAM-120, in the presence of Rg5, and in the absence of these compounds. As indicated in the table, more than 82% of the cells were still viable when grown in the presence of Rg5. However, less than 62% of the cells were viable when grown in the presence of PAM-120. Therefore, the compound PAM-120 is a better inhibitor of lung cancer cells than Rg5.

In paragraph 9 of his affidavit, Mr. Huang avers that he conducted experiments to compare the efficacy of PAM-120 and Rg5 against drug-resistant breast cancer cells. Mr. Huang measured the IC50 value of the compounds. This is the concentration of compound

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needed to reduce the growth of the cell population by 50%. The results from these experiments are reproduced below in Table 2 for the Examiner's reference.

Table 2: IC50 Values of Compounds PAM-120 and Rg5 against MCF7r Breast Cancer Cells

Compound	IC50 (:g/mL)
PAM-120	<10
Rg5	70 ± 5.4

The results indicate that the IC50 of PAM-120 is *more than 7 times lower* than the IC50 of Rg5. This indicates that a much lower concentration of PAM-120 is required to inhibit breast cancer cells than Rg5.

In paragraph 11 of the Mr. Huang's affidavit, Mr. Huang avers to the results of experiments conducted to compare the efficacy of PAM-120 and Rg5 against melanoma cells. Again, the IC50 of the compounds was determined. The results from these experiments are reproduced below in Table 3 for the Examiner's reference.

Table 3: IC50 Values of Compounds PAM-120 and Rg5 against B16 melanoma Cells

Compound	IC50 (:g/mL)
PAM-120	<10
Rg5	35 ± 3.9

The results indicate that PAM-120 has an IC50 that is *more than 3 times lower* than the IC50 of Rg5 against melanoma cells. This indicates that a much lower concentration of PAM-120 is required to inhibit melanoma cells than Rg5.

The above results indicate that PAM-120 has greater efficacy than Rg5 against various types of cancer cells. Although the Examiner asserts that the prior art compound Rg5 has anticancer activity, the above-results indicate that PAM-120 has superior anti-cancer activities. Accordingly, PAM-120 is not obvious in light of Rg5.

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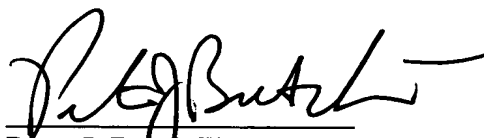
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The Applicant submits that it has complied with the Examiner's request for side-by-side comparisons of the compounds PAM-120 and Rg5. The Applicant also submits that it has now provided the Examiner with side-by-side comparisons of PAM-120 against all of the compounds Rg3, Rh2, and Rg5, which are referred to in the cited references and which the Examiner has cited. The results from the side-by-side experiments indicate that PAM-120 has greater effect against cancer cells than Rg3, Rh2, and Rg5. Accordingly, the Applicant submits that the subject matter of claim 9 is not obvious in light of the cited references and respectfully requests allowance of claim 9.

In light of the foregoing, the Applicant submits that both claims 9 and 10 are in condition for allowance, which is respectfully requested.

Respectfully submitted,

March 9, 2005

  
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APPENDIX "A"

Pursuant to 37 C.F.R. 1. 132, the Affidavit of Mr. Dong Huang, sworn 7 March 2005, is attached hereto.



APPENDIX "B"

Pursuant to 37 C.F.R. 1. 132, the Affidavit of Mr. Dong Huang, sworn 10 May 2004, is attached hereto.